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Breast Carcinoma Presenting with Thymic Metastasis: A Case Report

Timik Metastaz ile Prezente Olan Meme Karsinomu: Bir Olgu Sunumu

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Abstract

The thymus is a primary lymphoid organ located in the superior and anterior mediastinum. Thymic tumors constitute almost all anterior mediastinal tumors. Although thymomas are the most common tumors of the thymus in adults, metastasis of a tumor to the thymus is extremely rare. The diagnosis of space-occupying formations in the thymus is often made by clinical and radiological findings. It is confirmed by histopathological examination. In this article, a case of breast cancer with solitary thymus metastasis observed in the 9th year after mastectomy is presented.

Keywords: Breast cancer, thymic metastasis, thymus neoplasm, mediastinum

Öz

Timus, superior ve anterior mediastinumda yerleşik primer lenfoid bir organdır. Anterior mediastinal tümörlerin neredeyse tamamını timik tümörler oluşturmaktadır. Timomalar, erişkinlerde timusun en sık görülen tümörleri olmakla birlikte, timusa bir tümörün metastazı oldukça nadirdir. Timustaki yer kaplayan oluşumların tanısı sıklıkla klinik ve radyolojik bulgular ile konur ve histopatolojik inceleme ile kesinleşmektedir. Bu yazıda mastektomi sonrası 9. yılda soliter timus metastazı gözlenen meme kanseri tanılı bir olgu sunulmaktadır.

Anahtar Kelimeler: Meme kanseri, timik metastaz, timus neoplazm, mediasten

Introduction

The thymus gland is an organ responsible for cellular immunity located in the anterior mediastinum. Therefore, the probability of a tumor metastasizing to the thymus is considered very low⁽¹⁾. Although thymic tumors are rare, they constitute the majority of anterior mediastinal tumors. There are relatively few reports of thymic metastases^(1,2). However,

cases of breast, stomach, larynx, and lung cancer metastatic to the thymus have been reported in autopsy studies. In this case report, a breast cancer case with solitary thymus metastasis mimicking thymoma due to its rarity is presented.

Case Report

A 42-year-old female patient was admitted to the general surgery outpatient clinic in 2012 due to a palpable mass



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in her left breast. Invasive ductal carcinoma was detected because of tru-cut biopsy of the Breast Imaging Reporting and Data System 5 main mass localized in the outer quadrant of the left breast. Left partial mastectomy and axillary dissection were performed on the patient who did not detect distant metastases in the thorax and abdomen computed tomography (CT) performed on 4.07.2012. Mastectomy material is compatible with invasive ductal carcinoma and immunohistochemical staining results show 20% estrogen receptor (ER), progesterone receptor (PR) (-), c-erb-B2 (-), Ki-67 proliferation index 20%. The tumor was 1.9 cm in diameter and reported as lymph node metastasis (20/37) as a result of axillary lymph node dissection. The tumor was staged as T1N3M0 according to the TNM 7th edition classification.

The patient received 6 courses of docetaxel (75 mg/m²), doxorubicin (50 mg/m²), cyclophosphamide (500 mg/m²) and then radiotherapy as adjuvant treatment. Adjuvant tamoxifen (20 mg/day) treatment was applied for 4 years. Then letrozole (2.5 mg/day) treatment was administered. After the patient's 9th year follow-up after mastectomy, interstitial prominence and hilar fullness in PA AC X-ray and heterogeneous lobulated contoured mass formation in thymic localization in the anterior and upper mediastinum in the desired thorax CT were observed (Figure 1). The lesion surrounded the vascular structures, and especially the left brachiocephalic vein lumen was severely narrowed. No metastatic focus was observed on abdominal CT. The mass located in the upper and anterior mediastinum was sampled with an 18 G thick tru-cut biopsy needle using an automatic gun from the left parasternal area with anterior intervention under CT guidance. The biopsy result was consistent with breast carcinoma metastasis. Immunohistochemical staining of the lesion was evaluated as ER 2-3%, PR (-), c-erb-B2 (-), GCDFP-15 weak (+), GATA-3 (+), mammoglobin (-), p40 (-) and TTF-1 (-). CD5, CD70 and CD117 negativity also removed it from the thymic origin. However, it was considered inoperable because the mass invaded major vascular structures. Capecitabine was started at 2000 mg/m² (14 days use and 1 week interval) and was followed up closely. The patient is still receiving the current treatment. If the mass becomes operable, it is planned to be evaluated in terms of thymectomy.

Discussion

Cancer metastases to the thymus are extremely rare. Clark⁽³⁾ In a mouse study, it was reported that the blood-thymus barrier protects the thymus tissue from tumor cells and

antigens and prevents metastasis from cancer. However, the septum of the thymus consists of interlobular connective tissue with blood vessels, lymphatic drainage, and nerves, which theoretically excludes the possibility of metastasis. Therefore, the probability of thymic metastasis from tumors is low.

Together with the bone marrow, the thymus forms the organs where T lymphocytes are produced and differentiated. T-cell immunity is critical for controlling cancer formation, recurrence, and antitumor immunity. There has been recent progress on how abnormal thymic function affects cancer. The thymus causes decreased production of naive T-cells and limited T-cell receptor (TCR) diversity, resulting in immune senescence. It reduces the immune surveillance of neoplasia. In addition, regulatory T (Treg) relatively increases

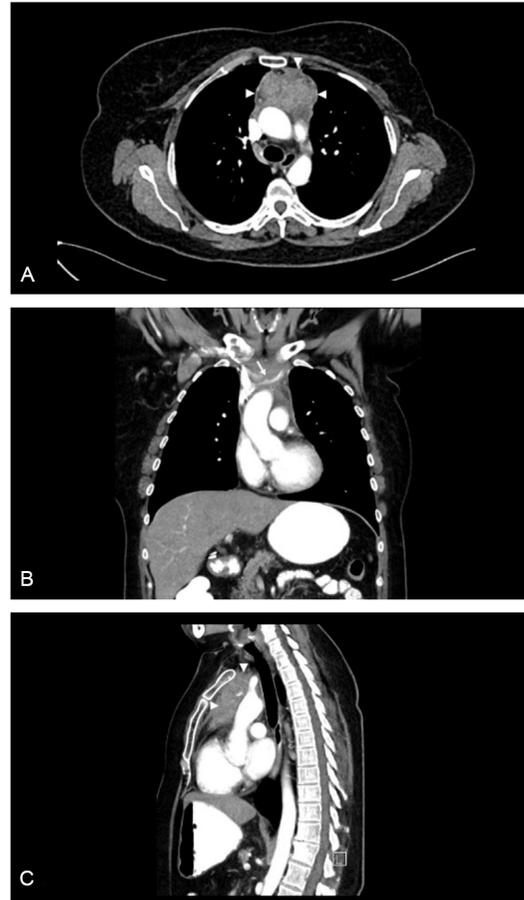


Figure 1. A) Axial image, B) coronal image, C) sagittal image. In contrast-enhanced thorax CT, a heterogeneous contrasting lobulated contoured mass filling the anterior mediastinum (white arrow) causes compression in the left subclavian vein, narrowing the lumen and surrounding it
CT: Computed tomography

the cell formation. In addition, acute thymic involution from chemotherapy may create a tumor reservoir resulting from an inflammatory microenvironment that is favorable for the storage of tumor cells that have spread in the thymus to survive chemotherapy. This may result in metastatic recurrence of cancers⁽⁴⁾.

It is important to distinguish between malignant thymic neoplasms and metastases. Almost all malignant neoplasms arising in the thymus have histological patterns that are also seen in primary tumors of other organs. These include keratinized and non-keratinized squamous, lymphoepithelioma-like, adenosquamous, clear cell, papillary, mucinous, mucoepidermoid, sarcomatoid, rhabdoid, micronodular, lymphoid-rich, and anaplastic morphotypes. Most thymic carcinomas are immunoreactive for both p63 and PAX8, unlike their extrathymic counterparts. Tumors lacking one or the other of these markers are immunohistochemically indistinguishable from metastatic lesions. Accordingly, a thorough radiological examination is necessary before a definitive diagnosis can be made⁽⁵⁾.

The thymus produces various peptide thymic hormones, including thymosin, thymopoietin, thymulin, and thymic humoral factor. It has been determined that these hormones play a role in immunological activity and tumor development. Shi et al.⁽⁶⁾ showed that thymic function affects breast cancer development and metastasis by regulating the expression of thymus secretions *PTM α* and *T β 15b1* genes. In addition, chemokine-autocrine signaling of thymus tissue may contribute to carcinogenesis and metastatic potential. *In vivo* experiments in rats showed that breast cancer cells can also secrete thymus-related chemokines in an autocrine fashion. As a result, epithelial-mesenchymal transition may be facilitated, cellular migration, tumoral invasion, and proliferation may be triggered, and apoptosis may be inhibited⁽⁷⁾.

Cases of breast, stomach, larynx, thyroid, and lung cancer metastatic to the thymus have been reported. During the two-year period from January 1963 to January 1965, the thymic tissues of 180 patients were examined in autopsies performed at the Brisbane Hospital, and 7% thymic metastases were observed in 102 carcinoma cases. Thymic metastases were detected in 4 patients with primary breast cancer⁽⁴⁾. In a retrospective 15-year autopsy data analysis published in 1979 by Cifuentes and Pickren⁽⁸⁾, the rate of metastatic thymus involvement was 11% (75 cases) in 707 cases with breast cancer⁽⁵⁾. It is difficult to distinguish thymic

metastases of breast cancer from imaging studies. The characteristic imaging findings of cancer metastasis to the thymus for diagnosis are not clearly known.

Takeuchi et al.⁽⁹⁾ reported that 284 of 1116 patients with breast cancer experienced recurrence after surgery and only 12 of 284 patients 10 years after surgery. Lymph node metastasis was detected in 10 of 12 patients with late recurrence at the first operation. This suggests that lymph node metastasis in the early onset of breast cancer is closely associated with late recurrence⁽⁶⁾. In this case, there was lymph node metastasis at the time of diagnosis, and distant metastasis to the thymus was observed 9 years after the operation.

The optimal management of these rare patients has not been clearly established. In general, surgical indications for metastatic breast cancer are palliative. However, the biology of the new tumor is learned from the pathological data to be obtained by surgery and the distinction between primary and metastatic tumors becomes clear. On the other hand, it has also been shown that resection of a small number of metastases from a single organ may contribute to long-term survival^(7,10). In the literature, reports on thymic metastasis of breast cancer gave information about the prognosis after thymectomy, and long-term survival was observed in the results^(7,10). In the report presented by Fujioka et al.⁽¹¹⁾, thoracoscopic thymectomy was performed in a case of luminal A breast cancer with thymic metastases. Aromatase inhibitor was started after surgery. It has been reported that the patient did not follow distant metastases for more than 36 months and the carcinoembryonic antigen returned to the normal level⁽⁷⁾. Fukunaga et al.⁽¹²⁾ applied chemotherapy and hormonal therapy after thymectomy to a breast cancer case with thymic metastasis, which was observed 13 years after surgery. It has been reported that the patient has lived for 6 years after thymectomy⁽⁸⁾.

Thymic epithelial cells have cytoplasmic ERs and estrogen regulates a normal cellular differentiation process indirectly via its receptor in the thymus. Estrogens depress thymosin release from the thymus, leading to thymus involution. Oyan et al.⁽¹³⁾ reported a well-differentiated thymic carcinoma detected in the 8th month of adjuvant tamoxifen (20 mg/day) treatment in a breast cancer patient. Thymoma secondary to breast cancer may be related to the anti-estrogenic effects of tamoxifen and possibly to the mutagenic effects of radiation on the epithelial cells of the thymus.

Park et al.⁽¹⁴⁾ described a case of invasive ductal breast carcinoma that metastasized to the thymus at the time

of diagnosis. Moretto et al.⁽¹⁵⁾ also reported a rare case of tumor-to-tumor metastasis to thymic epithelial tumor metastatic invasive ductal breast carcinoma. Metastasis of breast cancer to the thymus is rare, and it is important to recognize an unusual pattern of breast cancer metastasis in order to provide accurate, prompt diagnosis and appropriate treatment.

Ethics

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions

Surgical and Medical Practices: E.B.E., F.E., F.C., A.P.E., G.G., Concept: E.B.E., F.E., F.C., G.G., Desing: E.B.E., A.P.E., G.G., Data Collection or Processing: F.E., F.C., Analysis or Interpretation: E.B.E., A.P.E., Literature Search: E.B.E., F.E., Writing: E.B.E., F.E.

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